REMARKS

Status of the Claims

Claims 26, 28, 29, 54-60, 66-68, 70-78 and 80-82 are pending in the application.

Summary

Claims 26, 28, 29, 54-60, 66-68, 70-78 and 80-82 are pending in the application and were examined in the Office Action dated 2 June 2009 where the Office has maintained the following claim rejections: **(a)** claims 26, 28-29, 66-68, 70-71, 75-78 and 80-82 have been rejected under 35 U.S.C. §103(a) as unpatentable over International Publication WO 97/38698 to Manning et al. ("Manning"); **(b)** claims 54-60 have been rejected under 35 U.S.C. §103(a) as unpatentable over Manning; and **(c)** claims 72-74 have been rejected under 35 U.S.C. §103(a) as unpatentable over Manning in view of U.S. Patent No. 4,472,394 to Peterson ("Peterson"). Applicants respectfully traverse all pending claim rejections for the following reasons.

The Rejections under 35 U.S.C. §103

Claims 26, 28-29, 66-68, 70-71, 75-78 and 80-82 have been rejected under 35 U.S.C. §103(a) as unpatentable over Manning. In support of its rejection, the Office asserts that Manning "discloses using a carrier material in the form of a gel composition system that is 'capable of maintaining its position in order to provide a surface that substantially contacts the round window membrane of the middle ear ... [c]learly, the gel has enough support to maintain a shape for a period of time [and the Office] notes that the applicant has claimed a broad range of shapes that the gel of Manning could certainly embody." Office Action at page 6. Applicants respectfully disagree.

In pertinent part, 35 U.S.C. §103 provides that a patent may not be obtained "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious to a person having ordinary

skill in the art." 35 U.S.C. §103. Any analysis under Section 103 must consider the following factual inquiries: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) secondary considerations of non-obviousness (such as commercial success and long-felt but unsolved need, failure of others, and unexpected results). *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, (1966) (the "*Graham* factors"). The Supreme Court, in *KSR Intern. Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007) reaffirmed that the *Graham* factors "continue to define the inquiry that controls" an obviousness analysis.

Applicants recite novel methods for treating ear conditions where a drug delivery unit having a structure and shape is inserted directly into the round window niche so as to be positioned (and remain) within the round window niche. Applicants specify that the drug delivery unit is configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, strand, or plug. The Office asserts that the gel described by Manning "would maintain a shape for a period of time" and that such a shape could possibly embody one of applicants' recited structures. This assertion is incorrect. Manning expressly teaches that their compositions are "fluid enough to be injected through a fine gauge needle" (see Manning, page 5, lines 24-30). A fluid has no shape since the molecules in the fluid are free to move around. In addition, the Manning composition is a liquid (in this regard, applicants presume the Office does not take the position that the Manning composition is a fluid that is in the form of a gas). A liquid will flow but, unlike a gas, a liquid will not always fill every space within a container. The flow properties of a liquid depend upon a variety of factors including surface tension, viscosity and the like. Accordingly, it is simply not possible for the Office to support its position that the liquid of Manning would take the shape of a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, strand, or plug for even a transient moment. This is because the Manning composition has no shape, much less a defined shape such as applicants' recited device. Applicants respectfully submit that the Office seems to have mixed up the concept of fluid flow with that of actual structure and shape of a material.

Since the liquid composition of Manning cannot, by definition, have any shape, the Office cannot support a position that Manning actually discloses shaped compositions. The Office must therefore be relying upon some sort of inherency theory to support its position that Manning could have a shape for a transient period of time, and that shape could possibly embody one of applicants' recited structures. However, applicants note that the burden of proof for any assertion of inherency is exceptionally high. The fact that a certain result or characteristic may occur, or may be present in the prior art is simply not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999), emphasis added.

In the instant rejection, it is clear that the Office's assertion that Manning's liquid could inherently embody one of applicants' recited shapes falls far short of the requisite showing that Manning's liquid would necessarily have one of those shapes and that this shape would be recognized by a person of ordinary skill in the art. Contrary to the Office's assertion, the Manning composition does not have any shape at all, much less applicants' recited shape. In order to meet its burden in establishing a rejection under 35 U.S.C. §103 the Office must first demonstrate that the cited art teaches or suggests all the claimed limitations (including applicants' recited shaped devices). *See Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342 (Fed. Cir. 2007). The Office has failed to demonstrate that Manning teaches all of applicants' claim limitations. Accordingly, Manning does not render applicants' claims obvious by any direct disclosure therein or when the gel compositions are properly considered under a theory of inherency.

In addition, applicants submit that a proper consideration of secondary considerations under a Graham Factor analysis provides further support for a conclusion of non-obviousness over Manning. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, (1966). As noted by the Federal Circuit, the presence of secondary considerations such as long-felt but unsolved need, failure of others and unexpected results "may often be the most probative and cogent evidence [of non-obviousness] in the record." *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983). Post KSR, the Federal Circuit has confirmed the strength of such considerations, noting that evidence of objective criteria showing non-obviousness, including unexpected results, is of "particular importance". *Ortho-McNeil Pharm., Inc. v. Mylan Labs, Inc.*, 520 F.3d 1358 (Fed. Cir. 2008).

Applicants' claimed methods are a significant improvement over the art such as Manning, where a therapeutic can now be very specifically inserted directly into the target niche, avoiding potential inadvertent and harmful delivery to other tissue (important if ototoxic compositions are used), and ensuring direct delivery through the round window membrane for the duration of the controlled delivery event (hours, days, or even months).

Manning's method entailed flooding of the middle ear with a volume of liquid that fills at least one quarter of the entire middle ear. Manning does not teach or disclose direct insertion of a shaped drug unit directly into the subject niche, rather Manning floods the middle ear and lets some of the therapeutic eventually reach the niche. In this regard, the Office has expressed confusion on this issue (Office Action at page 6). Here again, applicants emphasize that the majority of the therapeutic administered by Manning will not be contained within the round window niche (it is flooded into the entire middle ear with only a small portion actually reaching the round window niche), and therefore the majority of the therapeutic will not even contact the round window membrane. Manning's methodology is not efficient in that a majority of the therapeutic drains out of the middle ear within the first day of delivery, and Manning's methodology is not safe in that a very large amount of the therapeutic is administered to other parts of the middle ear where toxic agents can cause actual harm to the sensitive middle ear tissue.

Manning completely fails to teach or disclose administration of a shaped drug unit configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, strand, or plug. Manning does not teach the placement of drug delivery unit directly into the round window niche (Manning teaches flooding the entire middle ear so that a portion of the therapeutic will contact the round window membrane). As discussed herein above, this feature of applicants' recited methodology provides significant efficiency and safety advantages. Even though Manning would presumably have been aware of the issues of safety (toxicity) and efficiency, Manning completely failed to teach or suggest applicants' recited methodology. This is evidence of a long felt need with a failure by Manning to avoid such safety and efficiency issues. This is accordingly strong and compelling evidence of non-obviousness. Since Manning failed to teach or suggest placement of drug delivery unit directly into the round window niche, and instead taught flooding of a large portion of the entire middle ear instead, it cannot possibly have enabled applicants' recited methods. An utter lack of any teaching or suggestion cannot possibly be considered to be enabling.

For all of the foregoing reasons, then, the rejection of claims 26, 28-29, 66-68, 70-71, 75-78 and 80-82 under 35 U.S.C. §103(a) is improper. The Office has simply failed to identify any teaching or suggestion in Manning that would lead to applicants' recited methodology, using devices with applicants' recited shapes. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

Claims 54-60 stand rejected under 35 U.S.C. §103(a) as unpatentable over Manning. In particular, the Office again asserts that Manning "discloses the invention substantially as claimed," and that the selection of a biocompatible polymer "is not critical to the invention" and is thus a "mere design choice" (Office Action at page 4.) Applicants respectfully disagree.

As established herein above, Manning's method of flooding the entire middle ear cannot render applicants' recited methods of providing specially shaped and configured drug delivery devices that are inserted directly into the round window niche. Accordingly, there are simply no facts or evidence of record that establishes a *prima facie* showing of obviousness over Manning. Accordingly, the rejection of claims 54-60 under

35 U.S.C. §103(a) is improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

Claims 72-74 stand rejected under 35 U.S.C. §103(a) as unpatentable over Manning in view of Peterson. Here again, the Office again asserts that Manning "discloses the invention substantially as claimed," and then looks to Peterson for a teaching of implanting a pellet below the ear of a farm animal. (Office Action at page 5.) Applicants respectfully disagree.

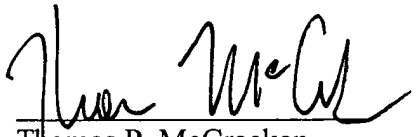
As discussed above, the primary reference to Manning does not even come close to teaching or suggesting applicants' novel methods. Applicants quite frankly do not follow the Office's reasoning that the Peterson implants could somehow overcome all of the shortcomings of Manning methodology, and lead to applicants' specifically shaped and configured drug delivery devices that are custom designed for insertion directly into the round window niche. There are simply no facts or evidence of record in this case that would support such an assertion. Accordingly, the rejection of claims 72-74 under 35 U.S.C. §103(a) is improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

CONCLUSION

Applicants submit that the pending claims define an invention that is both novel and nonobvious over the cited art, and thus all claims are in condition for allowance. Acknowledgement of this by the Office in the form of an early allowance is thus respectfully requested. In addition, if the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the Examiner to contact the undersigned at (408) 777-4915.

The appropriate fee is attached or authorized. If the Commissioner determines that an additional fee is necessary, the Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. **50-1953.**

Respectfully submitted,



Date: 1 July 2010

Thomas P. McCracken
Registration No. 38,548

For and on behalf of
DURECT CORPORATION
10240 Bubb Road
Cupertino, CA 95014
Phone: (408) 777-4915
Fax: (408) 777-3577